

**REMARKS**

Applicants are submitting herewith a Request for Continued Examination (RCE) and payment of the required fee along with the present Amendment which is the required submission for the RCE.

Applicants have amended claim 38 which corrects an obvious typographical error and incorporates the features of claim 44 into claim 38. Claims 42, 43 and 44 have been canceled from the application without prejudice or disclaimer. The claims now remaining in the application are claims 38, 40-41, 47-49 and 63. Applicants most respectfully submit that all of the claims now present in the application are in full compliance with 35 USC 112 and are clearly patentable over the references of record.

The rejection of claims 38, 40-44, 47-49 and 63 under 35 U.S.C. 103(a) as being unpatentable over Unger in view of Schneider and Martin have been carefully considered but are most respectfully traversed.

The Examiner's comments have been carefully considered by Applicants. However, Applicants wish to most respectfully draw the Examiner's attention to two key distinctions between the current claims and the disclosures of Unger. Reconsideration of the 103 rejection is respectfully requested in the light of the following comments and further amendments to the claims.

First, Unger refers exclusively to "fluorinated amphiphilic" compounds. This is a teaching in the reference as a whole and cannot be ignored. Consequently, the use of fluorinated compounds is clearly an essential feature of the Unger invention. For example, column 7, line 63 onwards, states:

"The fluorinated amphiphilic compounds, which are described in detail below, impart highly desirable properties to the compositions of the present invention. For example, it has been surprising and unexpectedly found that the fluorinated amphiphilic compounds are capable of stabilizing the present compositions ... are capable of promoting the formation of vesicles, as well as improving the stability of the formed vesicles."

Applicants have found that their agents do not have to be limited in this way and this clear teaching in Unger would lead one of ordinary skill in the art away from the presently claimed invention as now amended.



Secondly, Unger makes no reference to the use of one or more vector molecules, wherein said vectors bind to receptors/targets at sites associated with angiogenesis, inflammation, atherosclerotic plaques and/or thrombi. Unger merely refers to some examples of targeting materials as:

“proteins, including antibodies, carbohydrates, peptides, glycopeptides, glycolipids, lectins and nucleosides” (c.f. column 12, lines 48-49).

Clearly, the above passage does not suggest or teach to one of ordinary skill in the art the specific vectors claimed in the current patent application. Obvious to try is not the standard of obviousness under 35 USC 103(a).

With regard to the combination of the disclosures of Unger and Martin, the Examiner is respectfully reminded that Martin relates to an entirely different field of technology, i.e. that of drug delivery using fusogenic liposomes. It is most respectfully submitted therefore that the person skilled in the area of ultrasound contrast agents would not consider the disclosures of such a document to be relevant to the problem at hand, absent Applicants' teaching. In re Fritch, 23 USPQ 1780, 1784 (Fed Cir. 1992) (“It is impermissible to engage in hindsight reconstruction of the claimed invention, using the applicant's structure as a template and selecting elements from references to fill the gaps.”). Moreover, as just noted, obvious to try is not the standard of obviousness under 35 USC 103(a).

Furthermore, Martin discloses a variety of different vectors (e.g. Table 1, column 11), and there is no specific teaching in Martin to the subgroup of vectors claimed in the current application.

Similar comments can be made with regard to the relevance of a combination of the disclosures of Unger with Schneider. Schneider teaches an entirely different system from the currently claimed invention. That is, one where air or gas-filled microbubbles are formed in a suspension of liquid-filled liposomes, and where the liposomes apparently stabilize the microbubbles. Consequently, it is most respectfully submitted that the disclosures of this document and Unger would not have been combined together by the person skilled in the relevant area of technology. Accordingly, it is most respectfully requested that the rejection be withdrawn.



In view of the above comments and further amendments to the claims, and the filing herewith of a Request for Continued Examination, favorable reconsideration and allowance of all the claims now present in the application are most respectfully requested.

Respectfully submitted,

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**Marked-Up Version Showing Changes Made**

**IN THE CLAIMS:**

Please replace claim 38 with the following amended claim.

38(Twice Amended). A targetable diagnostic and/or therapeutically active agent comprising a suspension of a reporter comprising gas-filled microbubbles stabilized by monolayers of film-forming surfactant in an aqueous carrier liquid, and

wherein the gas comprises a halogenated gas or a halogenated low [molecule] molecular weight hydrocarbon, and

said film-forming surfactant comprises [a phospholipid] one or more phospholipids selected from the group consisting of phosphatidylcholines, phosphatidylglycerols, phosphatidylinositols, phosphatidylserines, phosphatidylethanolamines and phosphatidic acid, and

said agent comprising a lipid attached to a linker portion for covalent coupling to one or more vector molecules, and

where said vector(s) binding to receptors/targets at sites associated with angiogenesis, inflammation, atherosclerotic plaques and/or thrombi,

said linker portion optionally comprising a peptide linker portion.